culosis of the lungs. In the treatment of tuberculosis, when by the introduction of air into the chest cavity, the lung has been collapsed to allow it to rest and heal, radiography indicates the state of the lung and when it should be collapsed again. Pathological cavities in the substance of the lung are revealed by introducing into the chest lipiodol, which is an oil rendered opaque by iodising it. Radiography is a valuable aid in the study of heart disease. The heart is sometimes unexpectedly shown to be on the right side of the chest. In radiography of the brain, air may be introduced into the cavities of the brain, so locating and outlining in the radiograph the extent of a tumour and consequently indicating where the surgeon must operate.

The fine trabecular structure of the interior of

bones is plainly revealed by the X-rays. Difficult fractures are set under the fluorescent screen, thus assisting in producing perfect restoration of the damaged bone. The development of the human embryo is better understood, and radiographs of the unborn child show the centres of the ossification of the bones before birth and are often of invaluable assistance to the obstetrician.

The X-ray localisation of foreign objects in the body is a routine matter in hospitals, which are called upon to deal with an amazing variety of objects, for example, coins and safety-pins swallowed by children, dental plates inadvertently swallowed, nails, screws, safety razors, etc., deliberately swallowed by prisoners and others, and legacies from the War in the shape of buried bullets and shrapnel.

Genetics Since 1910

By PROF. J. B. S. HALDANE, F.R.S., Professor of Genetics, University College, London

THE state of genetical knowledge in 1910 can be learnt from Bateson's "Mendel's Principles of Heredity", of which the first two editions were published in 1909 and 1913. The principles which Mendel had shown to hold for seven contrasted pairs of characters in *Pisum* had been extended to a very large number of characters in many plant and animal species, including man. The main additions to these principles were the pure line, multiple allelomorphism, partial linkage between genes, epistasy, and one of the four types of sex linkage now known. The latter discovery, along with cytological work, had made the genetics of sex determination fairly clear. At least one case of extranuclear inheritance had been recorded.

Mendel's theory was based on the hypothesis that a (diploid) heterozygote produced two kinds of (haploid) gametes in equal numbers. This has since been proved in cases where the haploid generation has a number of variable characteristics; notably by v. Wettstein in mosses, or where individual haploids can be bred from, as by Andersson-Kottö in ferns. In such cases it is found that the products of a single meiosis are always exactly two cells carrying one member of an allelomorphic pair and two carrying the other. When several pairs are segregating, four different haploid types may arise, and a further analysis shows that genetic segregation may be associated with either meiotic division.

The cytological basis of genetics was cleared up by Morgan and his colleagues Bridges, Muller and Sturtevant, working on *Drosophila melanogaster*. They were able to show that the genes were located at different points on the chromosomes. Adequate

chromosome maps exist for several species of *Drosophila*, and, thanks largely to the co-ordinative work of Emerson, for *Zea Mays*. Less complete maps exist for *Lathyrus* (Punnett) *Pharbitis* (Imai) and other plants. By studying the giant chromosomes of the gland cells in *Drosophila*, Painter has been able to correlate the theoretically derived gene map with visible structure, and Muller and Prokofieva have detected visible changes associated with a difference affecting a single gene. Using chromosomes which were microscopically distinguishable owing to the attachment of sections of other chromosomes to them, Stern found that the visible changes in any individual could be predicted from its genetical constitution. Thus crossing-over is a physical fact as well as an explanation of genetical phenomena.

Similarly, Darlington has shown that there is a quantitative agreement between microscopically visible chiasmata and genetically detectable crossing-over, and has made it probable that these two events, which are really aspects of the same phenomenon, are both due to the relief of strains produced in the chromosomes by coiling. Equally striking is the cytological evidence that abnormal types of linkage are associated with cytologically visible exchanges of parts between different chromosomes (Muller and Altenburg, Hammarlund and Hakansson, Dobzhansky, McClintock, etc.).

Oenothera lamarckiana and other forms which breed nearly, but not quite, true, have been shown to be examples of permanent heterozygosis. Here the organism forms two kinds of gametes, but only one of the three possible combinations is produced, owing to inviability or competition.

The genetical analysis of *Oenothera* is mainly due to Renner, while Cleland, Darlington and other workers have elucidated its cytological basis, on principles largely suggested by Belling's work. Meanwhile Muller built up and analysed a *Drosophila* which behaved like *Oenothera*, possessing balanced lethal genes in two homologous chromosomes.

The genetics of polyploids are now understood. Gregory studied the genetics of the autotetraploid *Primula sinensis*, which contains four similar sets of chromosomes, and Winge pointed out that hybridisation might lead to an increase in the number of chromosome sets. The distinction between autopolyploids with more than two similar sets of chromosomes, and allopolyploids with several unlike sets of pairs derived from different species, was made by Kihara and Ono; while R. E. Clausen and Goodspeed, Newton and Pellaw, and many other authors analysed allopolyploids. Müntzing, by his synthesis of *Galeopsis tetrahit* from *G. pubescens* and *G. speciosa*, was the first to prove that Linnean species had arisen by hybridisation and doubling of the chromosome number. The gradual discovery that most cultivated plants are allopolyploids has given this work great practical importance.

The origin of new genes by mutation was a rare and uncontrollable process until Muller showed that it could be speeded up at least two hundred times by X-rays. Mutations generally lower the viability of an organism, but may raise it (Timoféeff-Ressowsky). They are generally recessive, but sometimes dominant. They are at least sometimes reversible by a further dose of X-radiation, and therefore cannot be regarded as mere injuries. They can also be provoked to a slight extent by heat, while the possibility of producing them by chemical agencies is still *sub judice*. The majority of mutant genes in animals appear to be lethal when homozygous. A proportion of these, including many so-called dominants, produce visible effects in the heterozygous condition.

In the normal type of sex determination one sex has two similar X-chromosomes, while the other has a single X, or more usually an X and a dissimilar Y. Besides genes carried by the X, the work of the last twenty-five years has disclosed others carried by the Y only (Schofield, Castle, Winge, Stern, etc.) or by both X and Y (Schmidt, Aida, Winge, de Zulueta, Philip, etc.). Genetical anomalies of sex linkage occurs in females with an added Y-chromosome (Bridges), with attached X-chromosomes (L. V. Morgan), translocations of sex-linked genes to other chromosomes, and so on. Bridges, by studying triploid *Drosophila*, showed that sex is determined not by the number of

X-chromosomes but by the balance between them and the autosomes. Thus animals with three sets of autosomes are females if they have three X-chromosomes, and intersexes if they have two. Goldschmidt showed that in *Lymantria* the X-chromosomes contain genes making for maleness, the cytoplasm and perhaps other constituents making for femaleness. By crossing geographical races of different sex potency he was able to produce intersexes or complete sex reversal. In *Lebistes*, Winge has been able to shift the sex-determining mechanism to a different pair of chromosomes, producing XX- or YY-males instead of the normal XY.

In Hymenoptera and some other groups the male is haploid. Here Whiting and others have shown that all genes behave like the sex-linked (X-linked) genes in man. But in *Habrobracon* at least, Whiting has proved that there is a further complication, the female being XY, the male X or Y, while X eggs are normally only fertilised by Y sperm, and conversely. Thus genes in the X- and Y-chromosomes show a fourth type of sex-linkage.

Finally, the Thallophyta have shown an astonishing variety of sexuality. V. Hartmann has found that in some flagellates sex is purely relative, a given type of gamete functioning as male with a less male partner, and conversely; while Kniep found two complementary sex pairs AB and ab, Ab and aB, in certain fungi, determined by two pairs of allelomorphic genes. Still more complicated cases exist, and it is very difficult to draw the line between sexes on one hand, and exogamous groups of self-sterile hermaphrodite plants, which may be determined as in fungi (Correns) or by series of multiple allelomorphs (East and Mangelsdorf, Lehmann and Filzer, Sirks, Brieger, Crane, etc.).

Much work has been done on individuals composed of two or more genetically different types of tissue, including mosaics, gynandromorphs, and plant chimæras. They may arise from grafting, double fertilisation, loss of a chromosome, mutation and so on. Among the most notable work is that of Morgan and Bridges on *Drosophila*, that of Jørgensen and Crane on *Solanum* and that of Imai on variegated plants.

Besides inheritance due to genes, extranuclear inheritance undoubtedly exists. The earlier work of Correns on the inheritance of abnormal plastid type has been extended, and other characters transmitted only by the seed parent have been recorded in plants. Little finds that the tendency to spontaneous cancer is largely inherited from the mother. However, Michaelis showed that in one such case the cytoplasmic influence gradually disappeared in the course of ten generations,

whereas genes in the nucleus show no such tendency. Jollos and Goldschmidt studied *Dauer-modifikationen* in *Drosophila* and other animals. These are changes of colour and shape produced by heat, and inherited from the mother only. Unlike mutant genes, they gradually disappear. A good many supposed cases of Lamarckian inheritance of acquired characters have been investigated. Many have been disproved, and none has been conclusively proved. However, the work of McDougall on rats and Sladden on *Carausius*, which suggest inheritance of acquired habits, are still under investigation.

Apart from these rather aberrant cases, there is increasingly strong reason to think that all heritable variation is due to genes. The evidence is particularly strong in *Drosophila* and *Zea Mays*, where characters determined by genes in several different chromosomes can readily be investigated by linkage tests. Fisher showed that the data of the biometric school on inheritance of human stature were consistent with the view that stature is determined by a number of genes, and the work of Punnett and his colleagues on inheritance of weight in poultry and rabbits confirms this view.

Human genetics has consisted largely of the accumulation of pedigrees. Very many genes are known. Thus Cockayne listed more than a hundred affecting the skin, hair or teeth. In addition to abnormalities, the antigens of the blood cells were shown by Landsteiner, Bernstein, Schiff and others to exhibit Mendelian inheritance. In the economic field, sex-linkage has been applied by Punnett, Pease and Crew to determine the sex of young birds on hatching, and genetic principles are used to eliminate recessive lethals in cattle and horses, and to produce new varieties of various plants. But the main economic effect has been from the gradual permeation of genetical principles among practical breeders, which has shown itself for example in the grading of bulls by their daughters' milk yield.

The physiological side of genetics was particularly developed by Goldschmidt, who showed that genes determine the form of the adult by affecting larval growth rates. Kraffka, Huxley, Zeleny, Plunkett and others have investigated the same problem. On the chemical side, Onslow, Garrod, Scott-Moncrieff, Brink and others have shown that in many cases a gene is responsible for some particular chemical process such as oxidation or methylation. The mechanism of segregation is itself controlled by genes (Beadle, Gowen, Frost, etc.), so that a change in one gene may affect the distribution of all the others.

On the other hand, little is known of the nature of the gene. An analysis of multiple allelomorphism shows that different modifications of the same

gene perform the same processes at different rates; however, in many cases it is certain that the genes do not consist of a number of like parts. At present the most hopeful line of attack on the fundamental problem of heredity, "How does one gene produce two like itself?", is to be found in the study of mutation, either natural, as in the work of Demerec and Andersson-Kottö, or provoked by X-rays. Andersson-Kottö's work suggests the possibility of distinguishing between a mother and daughter, or model and copy, in the products of gene 'division'.

A possibly important clue to the nature of gene action lies in the fact that, whereas most characters, for example, presence of an organ or a pigment, depend on the interaction of many genes, the presence of an antigen has so far always been found to be due to a single gene. Hence, except possibly in species crosses, no organism contains an antigen not found in either parent (Todd).

The cause of dominance has been much discussed. Bateson and Punnett regarded it as due to the presence in the dominant gene of something absent in the recessive; Fisher believes it to be an adaptive phenomenon due to modifying genes. Many workers take an intermediate point of view.

Naturally polymorphic populations have been investigated, especially by Nabours, Winge and Fryer. The genes concerned are often found to exhibit a surprising amount of linkage with one another. Tschetwerikoff, Dubinin, Spooner and others have shown that an apparently homogeneous population may include many individuals heterozygous for recessive genes producing very marked variations.

The species problem has been attacked from several sides. Vavilov pointed out that homologous variations in similar species generally show similar inheritance, but Harland has shown that there are exceptions to this law, and characters may occasionally be determined by different genes in related species. Sturtevant established a thorough-going parallelism in the action and arrangement in the chromosomes of genes in two allied *Drosophila* species.

The differences between some species appear to be mainly due to genes. In the rodents this is so for colour, and Green has located a gene responsible for part of the colour difference between two mouse species in a particular chromosome. Other species differ as regards the number and structure of their chromosomes, and here hybrids, if they exist, are often sterile. In particular, Blakeslee and his colleagues have compared the arrangement of the chromatin in a number of species of *Datura* from this point of view, while Babcock has done the same for *Crepis* and J. Clausen for *Viola*. On the

whole, it may be said that while we are fairly clear as to the nature of the genetical differences between related species, and it has been possible to imitate them within a single species (for example, by producing races which differ morphologically and will not cross), we are only rarely able to say with any certainty how species have originated in Nature.

The study of populations has developed a mathematical theory, due largely to Wright, Fisher, Bernstein, Haldane and Norton. The most important problems studied have been the effects on a population of inbreeding, selection, and

mutation, and the theory of estimation from samples. These involve among other things non-linear integrals and finite difference equations, and complex theorems in inverse probability. Their general result may be said to favour a modified Darwinian theory of evolution.

It must be emphasised that the main bulk of genetical research has been done by authors not named in this summary, and even where no new principles have been discovered, their work has shown that the general laws laid down by Mendel have as wide a validity for genetics as have Dalton's for chemistry.

Nuclear Structure and Chromosomes

By PROF. R. RUGGLES GATES, F.R.S., Professor of Botany, University of London

THE quarter-century of the King's reign has seen many striking advances in cytology, and particularly in our knowledge of the structure of the nucleus and its chromosomes. During the decade ending in 1910, the general theory of 'individuality' of the chromosomes had been established by the work of Boveri and others, the sex chromosomes had been discovered by McClung, and their general relation to sex determined, chiefly by the work of Wilson and his school. These remarkable beginnings definitely linked cytology with genetics and added strength to the view, already accepted in many quarters, that the chromosome reduction in meiosis furnished the physical basis for Mendelian segregation.

An equally notable line of research begun before 1910 was in determining the cytological basis of the mutations discovered by de Vries in *Oenothera*. This work laid the foundation for an analysis of mutations, so that by 1915 it was recognised that each mutation was in effect a cell change handed on by mitosis to every cell of the mutant. It was also recognised at this time that mutations could be classified into various types, which depended for their origin upon different kinds of chromosome change. The process afterwards known as non-disjunction had been discovered in the pollen mother-cells of *Oenothera rubrinervis* in 1908, and by 1912 it was proved that the mutant *Oe. lata* must have arisen by such a process, as it possessed an extra chromosome. Many other *Oenothera* mutations are now known to have an extra chromosome, and the conception of parallel mutations was founded upon the occurrence of *lata* and other mutations in different species.

These chromosomal mutations were regarded by many as convincing evidence of the chromosome theory of heredity. Recently (unpublished), trisomic ($2n + 1$) mutations have been found

occurring on a large scale in a wild species of *Oenothera*. Similar conditions have been observed by Huskins (1927) in fatuoid oats and speltoid wheats, plants with 40, 41, 42, 43 and 44 chromosomes being found where 42 is the normal number, but the exact relation between fatuoidy and the extra chromosome is still undecided. Blakeslee and his colleagues have recognised the twelve trisomic mutants to be expected in *Datura*, which has twelve pairs of chromosomes, as well as a series of secondary forms derived from exchange of segments in the primary trisomics.

In 1907-9 the mutant *Oenothera gigas* was recognised as a cell giant which had doubled its chromosomes. This was the beginning of the enormous modern field of polyploidy, or plants with chromosome multiples. The mutant *semi-gigas* was found to have 21 chromosomes (triploid) by Stomps and Lutz independently in 1912. Triploidy was discovered in *Drosophila* in 1921 and in *Datura* in the following year. While rare in animals, polyploidy is so widespread in flowering plants that a genus which does not show at least one case of it may almost be regarded as exceptional. Nearly all our cultivated plants, such as wheat, oats, sugarcane, cotton, apples, cherries, tomatoes, potatoes and pineapples, are now known to have varieties or species which possess different multiples of a particular basic number. Among wild species of roses, chrysanthemums, maples, horse-chestnuts, docks, violets, primroses, clovers, ragweeds, strawberries and many others, similar conditions prevail, so that the evolution of many plant genera has clearly been accompanied by the development of higher chromosome multiples from an original basic number, such as $b = 7, 9, 13$ or 17, for the genus. Where $2b$ is the ordinary (diploid) condition, some species may have $4b, 5b, 6b, 10b$, or occasionally even higher multiples.